

We claim:

1. A method of inhibiting the activation of a mammalian T-lymphocyte cell comprising: inhibiting *PTTG* expression and/or endogenous *PTTG* function in the T-lymphocyte cell, whereby activation of the T-lymphocyte cell is inhibited.
2. The method of Claim 1, further comprising delivering a *PTTG*-specific antisense oligonucleotide to the T-lymphocyte cell.
3. The method of Claim 1, further comprising interfering with SH3-mediated signal transduction by blocking specific binding to SH3-binding sites on endogenous *PTTG* protein molecules.
4. The method of Claim 1, further comprising:
delivering to the mammalian T-lymphocyte cell a composition comprising a *PTTG* carboxy-terminal-related polynucleotide, said polynucleotide being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to allow the polynucleotide to enter the cell, whereby activation of the lymphocyte cell is inhibited.
5. The method of Claim 1, wherein the T-lymphocyte cell is of human origin.
6. The method of Claim 1, wherein the T-lymphocyte cell is cultured in vitro.
7. The method of Claim 4, further comprising administering the composition to a mammalian subject, such that the composition is delivered to the lymphocyte cell in vivo.
8. The method of Claim 4, wherein the polynucleotide is a DNA or DNA analog.
9. The method of Claim 4, wherein the polynucleotide is an antisense oligonucleotide.
10. The method of Claim 4, wherein the polynucleotide is a protein nucleic acid.
11. The method of Claim 8, wherein the composition further comprises an expression vector comprising a promoter, and the *PTTG* carboxy-terminal-related polynucleotide is operatively linked to the promoter in a transcriptional unit.

12. The method of Claim 11, wherein the polynucleotide encodes a PTTG carboxy-terminal peptide.

13. The method of Claim 12, wherein the polynucleotide defines a nucleotide base sequence encoding a mammalian PTTG-C peptide selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

5 (B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or PTTG function.

14. The method of Claim 13, wherein the peptide fragment of (C) comprises a proline-rich region.

15. The method of Claim 13, wherein the polynucleotide has a nucleotide sequence consisting of

(A) (SEQ. ID. NO.:10), (SEQ. ID. NO.:18), or (SEQ. ID. NO.:19)

(B) a degenerate coding sequence of any of (A);

5 (C) a sequence complementary to any of (A) or (B); or

(D) a polynucleotide fragment comprising at least 45 contiguous nucleotides of any of (A), (B) or (C).

16. The method of Claim 1, comprising:

delivering to the mammalian T-lymphocyte cell, a composition comprising an expression vector comprising a promoter and a polynucleotide, said polynucleotide comprising a first DNA segment encoding a mammalian PTTG-C peptide, said polynucleotide being operatively linked to the promoter in a transcriptional unit; said PTTG-C peptide being selected from the group consisting of

5 (A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

(B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

10 (C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or *PTTG* function,

said expression vector being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the lymphocyte cell, such that the *PTTG*-C peptide is expressed in the T- lymphocyte cell, whereby activation of the lymphocyte cell is inhibited.

17. The method of Claim 16, wherein the peptide fragment of (C) comprises a proline-rich region.

18. The method of Claim 16, wherein the polynucleotide further comprises a second DNA segment encoding an uptake-enhancing and/or importation-competent peptide segment.

19. The method of Claim 18, wherein the cellular uptake-enhancing and/or importation-competent polypeptide is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.

20. The method of Claim 16, further comprising administering the composition to a mammalian subject in need of treatment, such that the expression vector is delivered to the lymphocyte cell in vivo.

21. The method of Claim 1, further comprising:
delivering to the mammalian T-lymphocyte cell a composition comprising a *PTTG* carboxy terminal peptide, or a biologically functional fragment thereof, complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the T-lymphocyte cell whereby activation of the
5 T-lymphocyte cell is inhibited.

22. The method of Claim 21, wherein the lymphocyte cell is of human origin.

23. The method of Claim 21, wherein the composition is delivered to the lymphocyte cell in vitro.

24. The method of Claim 21, further comprising administering the composition to a mammalian subject, such that the polynucleotide is delivered to the lymphocyte cell in vivo.

25. The method of Claim 21, wherein said uptake-enhancing agent is a polycationic lipid agent.

26. The method of Claim 21, wherein said uptake enhancing agent comprises a cellular uptake-enhancing and/or importation-competent peptide segment.

27. The method of Claim 26, wherein the cellular uptake-enhancing and/or importation-competent peptide segment is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.

28. The method of Claim 1, further comprising:
delivering to the human lymphocyte cell a composition comprising a PTTG-C peptide being selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

(B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or PTTG function,

said expression vector being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the lymphocyte cell, such that the PTTG-C peptide is expressed in the lymphocyte cell, whereby activation of the lymphocyte cell is inhibited.

29. The method of Claim 28, wherein the peptide fragment of (C) comprises a proline-rich region.

30. The method of Claim 28, wherein the composition is delivered to the cell in vitro.

31. The method of Claim 28, further comprising administering the composition to a human subject in need of treatment, such that the PTTG-C peptide is delivered to the lymphocyte cell in vivo.

32. The method of Claim 28, wherein said uptake enhancing agent comprises a polycationic

lipid.

33. The method of Claim 28, wherein said uptake enhancing agent comprises a cellular uptake-enhancing and/or importation-competent peptide segment.

34. The method of Claim 33, wherein the cellular uptake-enhancing and/or importation-competent peptide segment is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.

35. An in vitro method for screening substances for new immunosuppressive agents, comprising:

culturing mammalian T-lymphocytes;
exposing the cultured T-lymphocytes to a potential immunosuppressive agent in the presence of a known lymphocyte activator; and
detecting a change in the expression level of PTTG in the T-lymphocytes compared to control lymphocytes not exposed to the potential immunosuppressive agent, downregulation of PTTG expression being indicative of an immunosuppressive capacity possessed by the potential immunosuppressive agent.

36. A composition for inhibiting the activation of a mammalian T-lymphocyte, comprising a tamed HIV vector operatively linked to a PTTG carboxy-terminal-related polynucleotide.

37. The composition of Claim 36, wherein the polynucleotide encodes a mammalian PTTG-C peptide selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

(B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous PTTG expression and/or PTTG function, encoding a PTTG carboxy-terminal peptide and a

38. The composition of Claim 36, further comprising a pharmaceutically acceptable carrier.

39. The composition of Claim 37, wherein said PTTG carboxy-terminal peptide is selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

(B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or PTTG function.

40. The composition of Claim 36, wherein the polynucleotide is a DNA or DNA analog.

41. The composition of Claim 36, wherein the polynucleotide is an antisense oligonucleotide.

42. The composition of Claim 36, wherein the polynucleotide is a protein nucleic acid.

43. The composition of Claim 36, wherein the polynucleotide encodes a mammalian PTTG-C peptide or a complementary sequence.

44. The composition of Claim 43, wherein the polynucleotide defines a nucleotide base sequence encoding a mammalian PTTG-C peptide selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

5 (B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or PTTG function.

45. The composition of Claim 44, wherein the peptide fragment of (C) comprises a proline-rich region.

46. The composition of Claim 44, wherein the polynucleotide has a nucleotide sequence consisting essentially of

- 5 (A) (SEQ. ID. NO.:10), (SEQ. ID. NO.:18), or (SEQ. ID. NO.:19)
(B) a degenerate coding sequence of any of (A);
(C) a sequence complementary to any of (A) or (B); or
(D) a polynucleotide fragment comprising at least 45 contiguous nucleotides of any of (A), (B)
or (C).

47. The composition of Claim 36, further comprising an expression vector comprising the polynucleotide in a transcriptional unit.

48. A kit for the treatment of neoplastic cellular proliferation of T-lymphocytes, said kit comprising:
the composition of Claim 36; and
instructions for the use of said composition for inhibiting neoplastic cellular proliferation and/or transformation of T-lymphocytes.

49. A kit for immunosuppressive therapy, said kit comprising:
the composition of Claim 36; and
instructions for the use of said composition for inhibiting the activation of T-lymphocytes.

50. A kit for the treatment of neoplastic cellular proliferation of T-lymphocytes, said kit comprising:
the composition of Claim 37; and
instructions for the use of said composition for inhibiting neoplastic cellular proliferation and/or transformation of T-lymphocytes.

51. A kit for immunosuppressive therapy, said kit comprising:
the composition of Claim 37; and
instructions for the use of said composition for inhibiting the activation of T-lymphocytes.

52. The method of Claim 2, wherein the antisense oligonucleotide specifically binds to a regulatory region in the *PTTG* promoter selected from the group consisting of SSCA, 8182, a cyclic-AMP responsive element, an estrogen responsive element, an insulin response element, SP1, and a GC Box.

53. An in vitro method for screening substances for new immunoenhancing agents that enhance the activation of mammalian T-lymphocytes, comprising:

culturing the T-lymphocytes;

exposing the cultured T-lymphocytes to a potential immunoenhancing agent; and

detecting a change in the expression level of *PTTG* in the lymphocytes compared to control T-lymphocytes not exposed to the potential immunoenhancing agent, upregulation of *PTTG* expression being indicative of an immunoenhancing capacity possessed by the potential immunoenhancing agent.